(ii) Samples of the batch: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1*N* hydrochloric acid to obtain a concentration of 1,000 micrograms of doxycycline per milliliter (estimated). Further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous suspension containing the equivalent of 10 milligrams of doxycycline per milliliter.

(5) *Doxycycline content.* Proceed as directed in § 446.20(b)(5).

(6) *Identity.* Proceed as directed in § 436.211 of this chapter, using the 0.25 potassium bromide mixture described in paragraph (b)(1) of that section.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11155, Mar. 17, 1978; 45 FR 16476, Mar. 14, 1980; 50 FR 19920, May 13, 1985]

§ 446.42 Meclocycline sulfosalicylate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Meclocycline sulfosalicylate is the sulfosalicylate salt of 7-chloro-4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,10,12,12a-pentahydroxy-6-methylene-1,11-dioxo-2-naphthacenecarboxamide. It is so purified and dried that:

(i) Its potency is not less than 620 micrograms of meclocycline per milligram on an ''as is'' basis.

(ii) Its moisture content is not more than 4.0 percent.

(iii) Its pH is in an aqueous suspension containing 10 milligrams per milliliter is not less than 2.5 and not more than 3.5.

(iv) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on potency, moisture, pH, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the high-pressure liquid chromatography method shall be conclusive.

(i) *High-pressure liquid chromatography.* Proceed as directed in § 436.329 of this chapter.

(ii) *Microbiological turbidimetric assay.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 0.01*N* methanolic hydrochloric acid (solution 13) to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 0.06 microgram of meclocycline per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous suspension containing 10 milligrams of meclocycline per milliliter.

(4) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[46 FR 3836, Jan. 16, 1981]

§ 446.50 Methacycline hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Methacycline hydrochloride is [4S - (4α,4aα,5α,5aα, - 12aα)] - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11,12a - octahydro - 3,5,10,12,12a - pentahydroxy - 6 - methylene - 1,11 - dioxo - 2 - naphthacenecar - boxamide monohydrochloride. It is so purified and dried that:

(i) Its potency is not less than 832 micrograms of methacycline per milligram on an ''as is'' basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 2 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.0 nor more than 3.0.

(v) Its absorptivity at the absorption maximum of 345 nanometers relative to that of the methacycline working standard similarly treated is 92.4±4 percent.

(vi) It gives a positive result to the identity test for methacycline hydrochloride.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5(b) of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, absorptivity, identity, and crystallinity.

(ii) Samples of the batch: 10 packages, each containing 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient sterile distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.06 microgram of methacycline per milliliter (estimated).

(2) [Reserved]

(3) *Moisture.* Proceed as directed in §436.201 of this chapter.

(4) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 10 milligrams of methacycline per milliliter.

(5) *Absorptivity.* Determine the absorbance of the sample and standard solutions in the following manner: Dissolve approximately 50 milligrams each of the sample and standard in 100 milliliters of 0.01*N* methanolic hydrochloric acid. Transfer a 10-milliliter aliquot to a 250-milliliter volumetric flask and dilute to volume with 0.01*N* methanolic hydrochloric acid. Using a suitable spectrphotometer and 0.01*N* methanolic hydrochloric acid as the blank, scan the absorption spectrum between the wavelengths of 250 and 400 nanometers. Determine the absorbance of each solution at the maxima, ca. 345 nanometers. Determine the percent absorptivity of the sample relative to the absorptivity of the standard using the following calculations:

Percent relative absorptivity=(Absorbance of sample×weight in milligrams of standards×potency of standard in micrograms per milligram)/(Absorbance of standard×weight in milligrams of sample×10)

(6) *Identity.* The absorption spectrum between the wavelength of 250 and 400 nanometers, determined as directed in paragraph (b)(5) of this section, compares qualitatively with that of the methacycline standard.

(7) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11155, Mar. 17, 1978; 50 FR 19920, May 13, 1985]

§446.60 Minocycline hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Minocycline hydrochloride is [4S-(4α,4aα,5aα,12aα)]-4,7-bis (dimethylamino)-1,4,4a,5,5a,6,11, - 12a-octahydro-3,10,12, - 12a-tetrahydroxy-1,11-dioxo-2-naphthacenecarboxamide monohydrochloride. It is so purified and dried that:

(i) Its potency is not less than 890 micrograms per milligram and not more than 950 micrograms per milligram on the anhydrous basis.

(ii) [Reserved]

(iii) Its moisture content is not less than 4.3 percent and not more than 8.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams of minocycline per milliliter is not less than 3.5 and not more than 4.5.

(v) Its epi-minocycline content is not more than 1.2 percent.

(vi) It gives a positive identity test for minocycline hydrochloride.

(vii) It is crystalline.

(viii) Its residue on ignition is not more than 0.15 percent.

(ix) The absorptivity at 560 nanometers of an aqueous solution containing 10 milligrams of minocycline hydrochloride per milliliter is not more than 0.006.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.